the component county societies; and in the fulfillment of this duty I was inspired by the unity and the harmony in which the members of our profession are working. A politician once said: "Only once in every thirty years does the medical profession become sufficiently aroused to become a serious political factor; but when it does, it organizes and operates most effectively." The history of the past year of the profession in this State would seem to prove that he was right. Medical self-esteem has risen and harmony has been promoted, and we have been stimulated to repay, with even greater service, the confidence expressed by the people.

IN CONCLUSION

As we grow older, most of us become conservative, and some of us become reactionary. We must not let our natural conservatism blind us to the fact that we are living in an era of social and economic change, and that, as Grover Cleveland once said, "These are not theories that confront us; they are conditions." In the reasonable consideration of such problems as are confronting us today, it is most important to remember that change is not in itself bad, and that the fact that a thing is new is not a sound reason for its condemnation.

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RESEARCH IN MEDICINE: PRACTICAL APPLICATIONS*

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WE who are practicing medicine in this enlightened age at times are prone to look upon the methods employed by our predecessors in the profession with an attitude tinged with condescension. We often fail to realize the darkness through which they traveled, and the wonders which they accomplished with the few means at their disposal. The physician of ancient times, hindered in his progress by superstition and religious intolerance, and lacking the principles of the basic sciences from which so much of our knowledge has been derived, would look with awe upon the methods of diagnosis at our command, the vast array of conditions remediable by surgical intervention, and even the therapeutic equipment contained in the ordinary emergency bag of the present-day practitioner. It is the purpose of this paper to sketch briefly the manner in which this change in scientific endeavor was brought about, and what it has meant to the civilized world.

THE PRACTICE OF MEDICINE IN ANCIENT TIMES

The practice of medicine existed as a highly developed profession in Babylonia and in ancient Egypt, but direct care of the patient was associated with magic, witchcraft, superstition, and religion. Nevertheless, the Egyptians possessed a formidable materia medica, and many of the remedies have descended to our day. They originated the science of chemistry, and knew of the antiseptic value of extreme dryness as well as of chemicals such as niter and common salt. Egyptian medicine, however, languished and gradually merged with that of Greece.

THE DAWN OF RATIONAL MEDICINE

The dawn of rational medicine began in Greece under the influence and guidance of Hippocrates. He was the first to realize that disease was a part of the processes of nature, and was not divine in origin. With no other instruments than an open mind and keen senses, he classified diseases according to symptoms, emphasized the importance of careful observation, and was ever on the lookout for sources of error, which is the very essence of scientific spirit. Hippocrates was not acquainted with experiment, but he profited by experience. His description of epilepsy, puerperal sepsis, and other diseases would need but little change if printed in the textbooks of today.

Galen continued the Hippocratic method of observation and instituted the first experiments in physiology. Some of his anatomical descriptions were very good, but much of his talent was overshadowed by a tendency to obscure the facts by theoretical dogma. So profound was the effect of his teaching that, up to the time of Vesalius, his word was taken as final in any argument.

MEDICINE DURING THE DARK AGES

After Galen's death, European medicine remained at a standstill, and much was forgotten during the Dark Ages. However, at the time of the Renaissance, medical as well as other sciences were included in the great upheaval. New enthusiasm for Hippocrates and Galen began to flourish; this was largely due to the invention of the printing press. Rapid strides were made in the sixteenth and seventeenth centuries, and anatomy and physiology began to be studied intelligently. The greatest advancement during this period may be attributed to the book on anatomy by Vesalius in which he corrected many of Galen's misconceptions. Great was the furore aroused by this work, and it was many years before its true value was recognized.

THE BEGINNING OF MODERN MEDICINE

Modern medicine may be said to have originated at the time Harvey described the circulation of the blood. Although his discovery was of extreme value in itself, it opened a new field of medicine, for it was the first time that a definite medical problem had been solved by a combination of experimentation and observation. Following the example set by Harvey, rapid strides were made in the basic sciences, such as physiology, anatomy, chemistry, and physics. About this same time the invention of the microscope aroused a mild interest in the invisible world, but it was years before minute organisms and cellular changes in the tissues were associated with disease.

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On the other hand, the curative side of medicine remained in about the same stage as in the time of Hippocrates. The art of observation had been further developed and, as a consequence, many features of various diseases were known and the general knowledge of anatomy had increased. Linnæus set the vogue of classification in medicine as well as in botany, and from this time on, diseases were classified, symptoms were correlated, and descriptions of findings at necropsy were reported. Later, the names of Graves, Bright, Hodgkins, Addison and many others were intimately associated with diseases which were supposed to have been originally described by them. Nevertheless, these men only began to understand how the body functioned, for the cause of disease and rational methods of treatment were still unknown. One exception must be made, however: in 1796, Jenner demonstrated the value of vaccination in cases of smallpox, but one hundred years elapsed before the principles underlying acquired immunity were realized.

CONTRIBUTIONS DURING THE NINETEENTH CENTURY

About the middle of the nineteenth century many of the medical problems which had hitherto persistently resisted all attempts at solution gradually began to fall into their component parts after the discoveries made by Pasteur and Koch. Pasteur, a chemist, became interested in the field of biology through his studies of the fermentation of wine. At the conclusion of his successful work on the silkworm, which proved for the first time that biological problems could be solved by experimental methods, he was carried into the realm of bacteriology by an investigation on chicken cholera. His discovery of preventive inoculation was due to the accidental finding that virulent cultures of chicken cholera virus became inactive upon standing. He then observed that when the chickens which had failed to develop the disease were reinjected with material from fresh cultures, no untoward effects could be detected. When these principles were applied successfully in the treatment of anthrax in animals and hydrophobia in human beings, the science of immunology was born. In 1878 Koch introduced a new method of obtaining a pure culture, and conclusively demonstrated the relation of bacteria to disease. As a result of these discoveries greater advances were made in the next fifty years through experimental methods than had been accomplished in 2,500 years of observation.

DAWN OF MODERN SURGERY

The dawn of modern surgery, while closely related to the work of Pasteur and Koch, was ushered in by Lister, who was the first to visualize the possibilities of antisepsis in the operating room. It has often been said that surgery had almost reached the end of its progress when it was set free by Lister and his contributions, which have been of such great benefit to mankind. However, it should never be forgotten that the field of surgery would have been forever limited had it not been for the discovery of anesthesia. Thus, the surgeons in the nineteenth century, never lacking in skill and possessing a means of alleviating pain as well as a knowledge of the work of Pasteur and Lister, revolutionized their craft to such an extent that within a comparatively few years the entire body was included within its realm.

INFLUENCE OF THE SCIENCE OF BACTERIOLOGY

Before the time of Pasteur and Koch, so far as the curative side of medicine was concerned, there was little to light the pathway for the sick or for those who attended them. However, when microörganisms began to be definitely associated with disease, the minds of men received a new impulse, and their thoughts took a new direction. Consequently, great contributions were rapidly made by a long line of bacteriologists.

Only after the germ that causes *tuberculosis* had been discovered by Koch could mankind hope to eradicate this disease which has killed millions. Prophylactic measures, as well as new methods of treatment, were soon instituted and constantly improved, with the result that the changes in the mortality statistics in this country have been more promising from year to year.

Everyone is familiar with the large ward set aside primarily for the treatment of patients with *typhoid fever* in former days. This situation has entirely changed since the discovery of the Bacillus typhosus by Eberth in 1880. When it was found that chlorin killed the organism, chlorination of the city water supply eliminated one of the greatest sources of danger. In addition, the extensive use of vaccine prepared by Wright and Haffkine, and the improvements in diagnosis described by Widal, have been instrumental in lowering the death rate of typhoid fever to 1.5 per 100,000 of our population. As a result, so few are the cases seen at the present time that a medical student may see only one or two of these patients during the four years of his college course.

At the present time it is difficult to realize that *smallpox* used to claim 600,000 lives each year in Europe, and that in 1792 all of the population of the city of Boston had the disease except those who had had it previously. We have to thank the inquisitiveness and perception of our English country doctor for the methods at our disposal for control of the disease. While it had long been known that a patient who had suffered from cowpox never developed smallpox, no one realized the significance of the observation until Jenner published the results of his experiment. He had applied a small amount of cowpox virus, obtained from the lesion on the hand of a milkmaid, under the skin of a small boy; subsequently, when the boy was inoculated with smallpox virus, he failed to develop the disease. In this enlightened age everyone knows that, owing to the widespread practice of vaccination, smallpox is rare. On the other hand, how many realize that in the United States there were 48,000 cases of this disease in 1930, when there should have been none?

PREVENTIVE INOCULATION

The value of preventive inoculation against various diseases is well illustrated by what has been accomplished in the treatment of *diphtheria.* It is difficult to conceive practicing medicine today without an effective means of curing certain diseases. The new germs discovered in the throats of diphtheric patients by Klebs and Loeffler were found to produce a poison which was fatal when inoculated into animals. However, Behring observed that, if a non-fatal dose was administered, the animals eventually developed an immunity to the poison. He next noted that the blood serum of these resistant animals contained an anti-poison that neutralized the diphtheria poison. When he had successfully proved the value of this serum among human beings suffering from diphtheria, the scourge was chained that had been claiming the lives of half the patients afflicted, constituting thousands of individuals annually. Not many years afterward, following much experimentation on animals, science discovered toxin-antitoxin and toxoid which, when injected under the skin, renders the individual immune to the disease. Nevertheless, in the light of all this knowledge, there were 65,000 cases of diphtheria in this country in 1930. Only three hundred deaths from diphtheria in the city of Chicago was considered an excellent record in 1930; however, in 1933, the number of deaths was reduced to nine through the conscientious effort on the part of the physicians of that city in employing toxin-antitoxin and toxoid. This serves to indicate what might be accomplished by the organized medical profession supported by the public's coöperation.

At present we know more than ever before about the prevention and treatment of such diseases as *scarlet fever, whooping-cough, measles,* and *infantile paralysis.* This last has baffled scientists for many years, but, owing to recent investigations, we not only have a means of combating it, but we soon should be able to prevent by vaccination the crippling effects of this disease.

INSECT-BORNE DISEASES

The devastating epidemics of *malaria,* a disease known to Hippocrates and one that contributed to the fall of the Roman Empire, continued to ravage the civilized world until Laveran discovered the parasite in the blood of suffering patients, and Manson demonstrated the mosquito-malaria relationship. While the disease is still in evidence in swamp-ridden tropical countries, the death rate in America has been reduced to two per one hundred thousand inhabitants.

Following Manson's vision of insect-borne diseases, Reed, Lazear, Agramonte, and Carrol were appointed as a commission to investigate *yellow fever,* which was the disease that drove the populace out of Philadelphia soon after the Revolutionary War. After a prodigious and courageous search, during which Lazear lost his life while permitting himself to be used as an experimental subject, the etiologic agent of yellow fever was found to be carried by the mosquito (colopus). As a result of the commission's report, the United States Public Health Bureau, through the medium of rigid hygienic measures, has completely rid the country of this dangerous menace.

The knowledge of *protozoan and bacterial diseases* was put to a valuable test in 1904. Pestilence had played a large part in defeating past attempts to build the Panama Canal, and so the United States appointed a Health Commission to study the situation before it undertook the project. Malaria and yellow fever were banished, and dysentery was kept under control. In less than two years the mortality among the workers was materially reduced, being one-third of what it formerly had been. This is an excellent example of statesmanship directed by medical science.

Time does not permit a description of the methods by which typhus fever, the plague, and many other devastating diseases were conquered; nevertheless, sufficient has been said to indicate the extent of our indebtedness to the ones who carry out these researches.

THREE FACTORS IN THE DEVELOPMENT OF RESEARCH

Previous history having taught the value of experimentation, tremendous progress was made in our knowledge of the functions of organs and associated diseases not caused by bacteria. Research must advance through three essential steps before success is certain. After discovering the presence of a disease, its nature and cause must be determined. Usually the second step is to reproduce the disease in animals in order to learn how to prevent and treat it. Then, after the preliminary experiments in animals have been completed, the results are applied to man. In most instances success comes only after years of ceaseless, painstaking effort on the part of many men. Research cannot be hurried, for each man, before offering a contribution, must grope through darkened byways until the ultimate goal is reached and the average life span is increased one or two years more.

COMMENTS ON DISCOVERIES HAVING TO DO WITH CERTAIN DISEASES

Claude Bernard was the founder of the artificial production of disease by means of chemical and physical manipulation. It was he who coined the term "internal secretion," in describing his remarkable discovery of the *glycogenic function of the liver,* which has been of inestimable importance. Up to his time, gastric digestion constituted the sum total of the physiology of digestion. He cleared up the entire subject by showing that the gastric juice merely prepared the food for the digestive ferments produced by the pancreas, and he thereby laid the foundation for our studies on digestion and nutrition. In addition, the success which we have attained in the treatment of hypertension, Raynaud's disease, scleroderma, and other allied conditions, may be directly attributed to his discovery of the vasomotor mechanism.

The records of a Greek physician, Alexander Trallianus, show that *gall-stones* were recognized as an entity in the sixth century. In ancient times

bile and gall-stones were thought to cause remarkable cures when used as therapeutic agents. For instance, Rhases, an Arabian physician, about 900 A. D., wrote that the stones from the gall of an ox were ground up and drawn into the nostrils to promote sharpness of vision. If stones were not available, the bile of a black ox might be substituted. It was thought that if an animal had gallstones it was suitable for eating; but if the calculi had sharp edges, the animal was unfit for food. In the thirteenth century it was recorded that "some animals have no gall-bladder at all; some have the gall-bladder in the belly, and some have it in their ears." In ancient Babylon the idea arose that future events could be predicted by the condition of the gall-bladder of a sacrificial animal: if the right side of the gall-bladder appeared swollen, it pointed to an increase in the strength of the King's army. Swelling of the left side was considered an indication that the enemy was likely to be successful. In our day, mention of the biliary and digestive tracts recalls the names of Mann, Bollman, and their associates, for they have made some of the outstanding contributions to the knowledge of the physiology and pathology of the gall-bladder and liver. Mann was among the first to produce chronic peptic ulcer experimentally. This led to a more thorough understanding of the processes involved in the etiology and treatment of that condition. Their more recent studies on blood flow indicate that we may look forward confidently to revealing information on that subject.

All of us have friends who are enjoying life but who, except for the discovery of insulin, would be dead or existing only in a starved and miserable state. The cause of *diabetes* was established for the first time when, in 1889, two scientists removed the pancreas from a dog and produced this disease. However, it was not until a little more than ten years ago that Banting and his co-workers succeeded in isolating the hormone produced by the islands of Langerhans, which hormone is lacking in diabetic patients. Children having this disease formerly died in one or two years, but they now grow into healthy men and women. The life of adult diabetics has also been definitely prolonged. Statistics reveal that there are at least two million people in the United States alone who have benefited by this discovery.

That dreaded disease, *pernicious anemia,* has also been conquered in the past few years. The discovery of the value of liver therapy was the direct outcome of years of work by Whipple, Minot, Murphy and Robbins, who were endeavoring to learn the value of different diets in the treatment of experimental anemia in dogs and rats. As a result of their endeavors, thousands of individuals who formerly were doomed to slow but sure death can be maintained in excellent health at little inconvenience to themselves.

The advances in the mode of recognition and treatment of *diseases of the thyroid gland* during the past twenty years constitute a record of achievement as brilliant as any our age can boast. Parry, in 1825, and Graves, in 1835, gave accurate descriptions of hyperthyroidism, but it was not until 1886 that Möbius definitely ascribed the condition to an abnormality of the thyroid gland. The next step in advance was made by Müller, in 1893, when he found that the output of nitrogen in exophthalmic goiter considerably exceeded the intake. This was followed in 1895 by the work of Magnus-Levy, the outcome of which was a study of the basal metabolic rates of these individuals. Kendall finally succeeded in isolating thyroxin in crystalline form in 1914. Subsequent research by Kendall, Plummer, and Boothby resulted in the revelation that "thyroxin is a catalytic agent, hastening the rate of formation of a quantum of potential energy available for transformation on excitation of the cells." As a result of the combined efforts of these men, another drug was added to the therapeutic agents at the physician's disposal in the treatment of disease; for prior to this time the apathetic appearance and imbecility associated with myxedema were irremediable. Then, in 1922, Plummer introduced the use of iodin in the preoperative preparation of patients suffering from exophthalmic goiter. It may be said that this treatment with iodin has placed the surgery of exophthalmic goiter on a sound basis by reducing the severity of all of the manifestations of the disease, and by eliminating the long-feared and dangerous surgical complications. Thus the obstacles to surgery in this field finally yielded before the persistent efforts of a comparatively few men.

The *suprarenal glands,* regarded by the ancients as possessing miraculous powers and described by Addison from the clinical standpoint, are now known to produce at least two hormones. The value of one of these, epinephrin, has been demonstrated; but it was only recently that Kendall was able to isolate in crystalline form the other, which is essential to life. From his preliminary work with human beings as well as with dogs, it appears that yet another fatal disease has been mastered by providing substitution therapy.

Little was known of the minute parathyroid bodies until MacCallum demonstrated their relationship to calcium metabolism in 1908. Another twenty years went by before Hanson, a general practitioner interested in chemistry and working in his laboratory in spare moments, actually isolated the active hormone. Collip later substantiated Hanson's work, and proved the value of the preparation in the treatment of those unfortunate individuals suffering from parathyroid tetany.

In addition to the work already considered, that on the pituitary body, thymus, and sex organs, indicates that we may confidently look for even more revealing and valuable discoveries in these fields in the near future.

VALUE OF THE KNOWLEDGE ACQUIRED FROM THE EXPERIMENTS OF CHEMISTS AND CHEMICAL PHYSICISTS

As men of science, it is not difficult for us to appreciate the revolutionary changes in the civilized world which have resulted from the experiments conducted by the chemist and chemical

physicist. Without their aid the age of electricity would not have been possible, nor would we have the diagnostic and therapeutic uses of roentgen-rays or radium. The organic chemist has not only shed light on the complex processes occurring in the body, but has also produced many therapeutic agents. It is difficult for us to conceive of practicing without cocain, novocain, salicylic acid, acetanilid, eserin, pituitrin, salvarsan, and innumerable other drugs, all of which are of comparatively recent origin. A new era in the diagnosis and treatment of deficiency diseases was ushered in through the discovery, mainly by biochemists, of the vitamins which are so essential to life.

CIVILIZATION'S OBLIGATIONS TO RESEARCH WORKERS

This presentation has necessarily been brief, and many important findings have been omitted; likewise, much of the routine work has been overshadowed by the spectacular. However, we also wish to pay tribute to those individuals whose contributions have been of inestimable value to the medical profession. Some of the greatest contributions have been made by those who work single-handed while engaged in an active practice, and too often at great physical expense. In the present rather revolutionary period, many changes in our methods of practice have been suggested. Too often in time of turmoil the distractions outweigh the incentive, and it is impossible to progress with maximal efficiency. Research has been defined as "a method of keeping everyone reasonably dissatisfied with what he has." There never was a greater need for original investigation, or a better opportunity to salvage time for it than the present.

PURE SCIENCE INVESTIGATION AND CLINICAL OBSERVATION ARE BOTH IMPORTANT

Much has been written concerning the methods that should be employed in conducting original investigation, but it should be pointed out that, although there are some fields of study best left in the hands of the so-called pure scientists, research is not confined to the laboratory worker alone. Accurate observation of signs and symptoms, and their correlation with disease, will always be essential. In addition, there are certain phases of research which cannot be conducted by the laboratory investigator. The study of the earliest changes in disturbed function, which later develop into a definite clinical entity, lies solely within the realm of the family physician. Moreover, the science of prognosis and the evaluation of therapeutic remedies when applied to man necessitate an acuteness of observation during the progress of the disease which the scientists alone cannot appreciate. There can be no doubt that, although closely related, the fields to be conquered by laboratory methods and curative medicine are different. In order to progress with maximal efficiency, not only must observatory and experimental methods be coördinated, but there must also be an intimate contact between the investigators and the disease as it exists in man.

IN CONCLUSION

In conclusion, it seems to be in order to determine the results of all this knowledge which we have struggled so long and so diligently to obtain. One would be making a conservative estimate in stating that there are fifty million people in this country today whose lives have been saved or prolonged through medical science. While there are those who might question such an assertion, the figures are easily arrived at. One hundred years ago the average span of life was thirty-five years; today it is sixty. Since there are 126,000,000 people living in these United States, it is a simple problem to calculate the number of individuals whose existence at the present time is dependent upon the measures which have been instituted to prolong life. Moreover, seven years have been added to the average life span in the last twenty-three years, for in 1911 the average length of life was only fifty-three years. This also means that there are 13,000,000 people alive today who would have been dead but for the progress made in medical science. At the present rate of increase in knowledge, man can look forward to an average of sixty-five years of life by 1944. The battle in which we are active participants will never cease, for the diverse ramifications of our science are bound to hold our interest. However, it is the judicious employment of these days that will continue to advance the front of our knowledge during this period, and speed it on its way to even greater heights.

The Mayo Foundation.

THE DIFFERENTIAL DIAGNOSIS OF INTRACRANIAL DAMAGE*

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DISCUSSION *by Howard C. Naffziger, M. D., San Francisco; Carl W. Rand, M. D., Los Angeles; Howard W. Fleming, San Francisco.*

THE symptoms and signs of cerebral injury may result not only from intracerebral lesions, namely, concussion, contusion, laceration and intracerebral hemorrhage, but also from cerebral compression due either to depressed fractures, extradural or subdural hemorrhages.

DIFFERENTIAL DIAGNOSIS

The differentiation between these conditions is the essential point in determining the method of treatment.

Concussion.—Unfortunately in the past the term concussion has been used in a very elastic manner to include severe cerebral contusion and even laceration.

At present it is customary to designate as concussion head injuries in which no definite pathological changes are apparent.

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